REMARKS

With this amendment, claims 1-10, 13-21 and 24-28 remain pending in the application. Claims 5-7 and 18 have been amended to change "plasmin composition" to "plasmin" consistent with the antecedent basis provided in claim 1. With these amendments, the objections to claims 5-7 and 18 as to this informality are believed to have been addressed. Withdrawal of the rejection as to these claims is therefore requested.

The outstanding claim rejections include claims 1-4, 7-10 and 13 stand rejected in the alternative under 35 U.S.C. §102(b)/§103(a) over Gandorfer et al.; claims 1-10, 13-21 and 24-28 stand rejected in the alternative under 35 U.S.C. §102(b)/§103(a) over Trese et al. (Ophthalmology, Volume 107, No. 8, August 2000); claims 1-10, 13-21 and 24-28 stand rejected in the alternative under 35 U.S.C. §102(a)/§103(a) over Shi et al. A new basis for rejection is added in Paper No. 9302004 including the rejection of claims 1-7, 9, 10, 13-18, 20, 21 and 24-28 in the alternative under 35 U.S.C. §102(b)/§103(a) over Trese et al. (Ophthalmology, Volume 105, Issue 9, 1 September 1998, pages 1617-1620).

Remarks Directed to Rejection With Respect to Gandorfer et al.

Applicant hereby incorporates by reference the remarks of record with respect to this rejection. To summarize Applicant's position as to why this rejection is improper: Gandorfer et al. nowhere teaches a dose of less than 0.4 units of plasmin to induce vitreous liquefaction in a human eye and as such Gandorfer et al. is not anticipatory of the pending claims. The teachings of Gandorfer et al. indicate that a dosage of one unit of plasmin affords incomplete vitreoretinal separation while two units of plasmin proved successful. (See page 6, Abstract: Results). As such, one of skill in the art reading Gandorfer et al. would not be motivated to reduce the dose of plasmin below one unit to create vitreal liquefaction but instead increase the dosage certainly

above one unit of plasmin and more likely above two units of plasmin to perform the claimed procedure. Since Gandorfer et al. is teaching away from the claimed dosage of plasmin, Gandorfer et al. cannot render the pending claims obvious.

In light of the above remarks, withdrawal of the rejections as to the pending claims as obvious or anticipated by Gandorfer et al. is requested.

Remarks Directed to Claim Rejections Over Shi et al.

Applicant incorporates by reference the remarks of record with respect to this rejection. Applicant's position as to patentability of the pending claims over Shi et al. is summarized as follows: Shi et al. teaches the delivery of plasmin in doses of zero, one, two or three plasmin units in 0.1 milliliter injection volumes. Shi et al. notes successful vitreous detachment only for three units of plasmin (see abstract and page 61, right column, last paragraph). As Shi et al. does not teach the limitation of 0.4 units of plasmin to induce vitreous liquefaction, the pending claims are not anticipated by Shi et al. As Shi et al. attempted the use of lower dosages of plasmin to induce vitreous detachment (zero, one and two units of plasmin) and found the results unsatisfactory, one skilled in the art upon reading Shi et al. would lack motivation to use 0.4 units of plasmin to induce vitreous liquefaction as per the pending claims.

In light of these remarks, withdrawal of the rejection as to the pending claims with respect to Shi et al. under 35 U.S.C. §102(a)/§103(a) is solicited.

Remarks Directed to Rejections of Pending Claims With Respect to Trese et al. (Ophthalmology, Volume 107, No. 8, August 2000)

Applicant incorporates by reference the remarks with respect to this basis of rejection. Of record are declarations submitted under 37 CFR 1.132 by Patrick Gaffney and Michael Hartzer providing evidence that the inability to afford uniform vitreous liquefaction in human

eyes at a dose of 0.4 international units in the paper published in Ophthalmology, Volume 107, No. 8, August 2000 by Trese et al. at the same doses that are now claimed was attributable to the fact that what was thought to be plasmin in the Trese et al. article was in large part a plasminogen-streptokinase complex that has less activity than plasmin.

The Examiner has taken the position that this article should be read literally and that the declarations so provided carry no weight because "one of ordinary skill in the art would interpret the article to produce autologous plasmin since that is what is stated." (Paper No. 9302004, page 5, section 10).

Accepting a literal reading of this reference, the Applicant again directs the Examiner's attention to page 1610, left column, first full paragraph that states:

> The dose of 0.4 IU of autologous plasmin enzyme, which seems optimal for producing a PVD in humans, does not show the reliable liquefaction of vitreous that was seen in animals. . . . We believe that this study demonstrates that it is possible to achieve spontaneous posterior vitreous separation and closure of macular holes in the human eye but that liquefaction of the vitreous gel is variable in human eyes at the dose of 0.4 IU.

As such, Applicant submits that Trese et al., Ophthalmology, Vol. 107, No. 8, August 2000, while enabling for the closure of macular holes in the human eye, is in fact not enabling for liquefaction of the vitreous at a dose of 0.4 units. It is a well-established tenet of patent law that an anticipatory reference must enable the subject matter for which it was cited. The clear language of this reference shows that vitreous liquefaction is not reliably occurring in human eyes at a dose 0.4 units. As such, it is Applicant's position that this reference does not anticipate the pending claims.

Likewise, the clear language quoted above from Trese et al., Ophthalmology, Vol. 107, No. 8, August 2000 is submitted to not motivate one skilled in the art to perform vitreous

liquefaction with 0.4 units of plasmin. The plain language of this reference states that vitreous liquefaction at this dose of plasmin is unreliable in the human eye and implying larger doses are needed. Thus, should the Examiner refuse to give patentable weight to the statements found in the declarations of record, then the plain language of the reference is respectfully submitted to negate anticipation of the pending claims on the basis of lack of enablement for performing vitreous liquefaction at a plasmin dose of 0.4 units, or in the alternative, failing to provide one skilled in the art with motivation to perform vitreous liquefaction with this dosage of plasmin.

In light of the above remarks, reconsideration and withdrawal of the rejections as to the pending claims with regard to Trese et al. (Ophthalmology, Vol. 107, No. 8, August 2000) is solicited.

Remarks Directed to Rejection of Pending Claims Under 35 U.S.C. §102(b)/§103(a) Over Trese et al. (Ophthalmology, Vol. 105, Issue 9, 1 September 1998)

Trese et al. (Ophthalmology, Vol. 105) is cited as disclosing the delivery of autologous human plasmin into a vitreous body of an eye and after incubation within the eye removing the liquefied material. The reference is also cited as disclosing using 0.4 units thereby rendering it obvious to one of ordinary skill in the art to change the amount of enzyme used (Paper No. 9302004, page 4, section 7).

The pending claims all recite the limitation of creating a "liquefied vitreous".

Trese et al. (Ophthalmology, Vol. 105) is submitted to teach that autologous plasmin at 0.4 units represents "an adjunct to vitrectomy facilitated removal of the cortical vitreous from the retinal surface. Subsequent investigations are necessary to evaluate whether plasmin enzyme-assisted vitrectomy will decrease the incidence of surgical complications." (Final paragraph of reference). As Trese et al. (Ophthalmology, Vol. 105) nowhere teaches or contemplates vitreous

liquefaction but instead only teaches lessening vitreal adhesion to the retinal surface as part of a surgical procedure to remove the vitreous (vitrectomy), Applicant submits that Trese et al. (Ophthalmology, Vol. 105), based on the plain language of the reference, fails to enable vitreous liquefaction. If the Examiner disagrees with Applicant's characterization of Trese et al. (Ophthalmology, Vol. 105), then it is respectfully requested that it be stated with greater clarity why one would remove the vitreous as part of a vitrectomy when the vitreous has been returned to its normal liquefied state.

Applicant submits that one skilled in the art at the time of invention would not have been motivated to use 0.4 units of plasmin to perform the claimed inventive process since one skilled in the art would find no motivation to attempt vitreous liquefaction within Trese et al. (Ophthalmology, Vol. 105) but at best only to undertake experiments with respect to the use of plasmin as an adjunct to mechanical vitrectomy. Additionally, one skilled in the art upon viewing Trese et al. (Ophthalmology, Vol. 105), alone or in combination with the other prior art of record, would not to attempt vitreous liquefaction with 0.4 units but rather to attempt vitreous liquefaction with much higher doses of plasmin.

In light of the above remarks, withdrawal of the rejection as to claims 1-7, 9, 10, 13-18, 20, 21 and 24-28 under 35 U.S.C. §102(b)/§103(a) over Trese et al. (Ophthalmology, Vol. 105, Issue 9, 1 September 1998, pages 1617-1620) is solicited.

Summary

Claims 1-10, 13-21 and 24-28 are the claims pending in this application. Entry of this amendment is requested. Reconsideration and allowance of the claims is also solicited.

Respectfully submitted,

/ang/

Avery N. Goldstein
Registration No. 39,204
Gifford, Krass, Groh, Sprinkle,
Anderson & Citkowski, P.C.
280 N. Old Woodward, Suite 400
Birmingham, MI 48009
(248) 647-6000

Attorney for Applicant

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Janice R. Kuehn

Janice R. Kuehn